

REMARKS

Claims 62-78 are canceled, without prejudice or disclaimer. Claims 1-61 were previously canceled. New claims 79-90 are added. The new claims correspond to the subject matter of the previous claims, in particular claim 79 corresponds to the subject matter of former claims 62 and 65, and claim 86 corresponds to the subject matter of former claims 72 and 74.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. SPECIFICATION

The Examiner contends that the specification is still "somewhat confusing in the recitation 'may also be separated as follows, i.e., meaning the same as the plus sign Asp30Ala/Ser34Glu or N30A/S34E' as applicants have not maintained consistency with the first part of applicants amendment which recites 'Ala30Asp + Glu34Ser or A30D+E34S.'"

This rejection is respectfully traversed. The referenced paragraph clearly states that the recitation Ala30Asp + Glu34Ser or A30D+E34S (which use a plus "+" sign between the mutations) is equivalent to the recitation Asp30Ala/Ser34Glu or N30A/S34E (which use a slash "/" between the mutations). There is nothing confusing in this paragraph and the Examiner's statement that the two recitations lack consistency is not valid. The two phrases are simply suitable alternative recitations. If the rejection is maintained, the Examiner is requested to explain what is confusing, how it is confusing, and why an alternative recitation is not permitted in a patent application.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. Claim Objections

Claims 63, 69 and 76-78 are objected to as follows:

Claim 63 contains a superfluous "that." Applicants appreciate the Examiner's identification of this issue and claim 63 has now been amended to correct the duplicate use of the term "that."

The Examiner states that claims 62 and 73-78 further limit the claim from which they depend and should accordingly state "further comprising" instead of "comprising."

With respect to proposed use of the recitation "further comprising," the term "comprising" in claim 62 means that the claim is open to other alterations. Furthermore, a dependent claim, by definition, includes all of the limitations from the claim from which it depends. Thus, it is not clear

why the term "further" is necessary or would add any more clarity since the dependent claims define the same invention with the transitional phrase "comprising" as they do with the transitional phrase "further comprising." Nevertheless, the new claims employ the term "further comprising."

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 62-78 under 35 U.S.C. 112

Claims 62-78 are rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. The Examiner alleges that a skilled artisan is not capable of preparing nucleic acids encoding alpha amylases having an amino acid sequences which are at least 70% identical to SEQ ID NO:4, at least 80% identical to SEQ ID NO:4, at least 90% identical to SEQ ID NO:4, or at least 95% identical to SEQ ID NO:4 and which comprise an alteration at a position corresponding to position 356 or 376 in SEQ ID NO:4. The Examiner also contends that the artisan would apparently have to make and test an infinite number of nucleic acid sequences in order to practice the invention in a manner reasonably correlated with the scope of the claims.

The enablement rejection fails to give proper consideration to the evidence provided in the specification, the high level of skill in the applicable art, and to the fact that the alpha-amylase art is one of the most well characterized proteins known, with considerable knowledge about the structure of these enzymes and what changes can be made, including numerous three-dimensional structures provided in the art and numerous wild-type and variants sequences described.

Foremost, as disclosed in the specification, the alterations claimed provide improved properties to certain alpha-amylases, including the alpha amylase shown in SEQ ID NO:4. The alpha-amylase shown in SEQ ID NO. 4 is a member of a family of highly related alpha-amylases, referred to in the specification as the "Termamyl-like alpha-amylases", which, in addition to SEQ ID NO:4, include the alpha amylases shown in SEQ ID NOS. 1, 2, 3, 5, 6, 7 and 8.

As disclosed in the specification, there is an extensive body of both patent and scientific literature relating to alpha-amylases in general, and specifically, the Termamyl-like alpha-amylase family. This work contains a very detailed three-dimensional, X-ray crystal structure analysis, including identifying the domains and amino acids which make up the structure of Termamyl-like alpha-amylase. See, e.g., WO 96/23874. Because these alpha-amylases share substantial sequence similarity and a similar three-dimensional structure, alterations in

one member of the family can with a reasonably degree of certainty be applied throughout the family.

The patent and scientific literature also discloses many alterations which can be made to improve various properties of Termamyl-like alpha-amylases. For example, WO 96/23874, WO 97/41213, U.S. Patent No. 5,731,280, to name a few, discloses numerous alpha-amylase variants.

In this regard, an artisan can use any one of the numerous nucleic acid sequences encoding wild-type alpha-amylase (including SEQ ID NOS. 1, 2, 3, 4, 5, 6, 7 and 8) as well as nucleic acid sequences encoding variant alpha-amylases which are described in the art for preparing the nucleic acids encoding alpha-amylase having the recited alterations. Alternatively, the artisan can generate nucleic acid sequences encoding new alpha-amylases using, e.g., the mutagenesis techniques disclosed in the specification as starting material for preparing the nucleic acids encoding alpha-amylases having the recited alterations.

The claims are narrowly drawn to encompass a family of alpha-amylases which an artisan can expect with a reasonably high degree of certainty that the claimed alterations will apply. Some of the alpha amylase in the recited family may *possibly* not be suitable, however, this factor does not lead to a conclusion that the claims lack enablement given that the skilled artisan is able to prepare nucleic acid sequences encoding variants which have a degree of identity of at least 70% to SEQ ID NO:4 to vast number of species.

The conclusion that the claims lack enablement significantly short changes the advancement applicants have provided to the art and, more importantly, ignores the ability of the highly skilled artisan and the fact that the alpha-amylase art is so very well characterized.

The Examiner assertion that the artisan would have to produce an infinite number of nucleic acids and test them in order to practice the invention is also not an appropriate assessment. As a simple analogy, take a claim to a four legged chair. Such a chair could have the legs in various positions on the base of the chair. Certainly, when the legs are set in some positions, the chair would be unstable. However, the fact that the chair may be unstable when legs are placed in some positions does not mean that the artisan lacks enablement to build four legged chairs having legs in a variety of position and the artisan would have to make an infinite number of four legged chairs to practice the claimed invention.

Turning to the case at hand, though nucleic acid and protein engineering is arguably more complex than many four-legged chair building practices, the skill in the art is very high and both applicants' specification and the volume of publications evidencing the ability of the artisan

to make nucleic acid sequences encoding variants having at least 70% to SEQ ID NO:4 establish that an artisan can produce such nucleic acid sequences encoding variants which have the claimed alterations.

Notwithstanding the above, in order to expedite prosecution the claims now recite that the nucleic acid sequence encodes a variant having an amino acid sequence which is at least 90% identical to SEQ ID NO:4.


For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: June 7, 2004



Jason I. Garbell, Reg. No. 44,116
Novozymes North America, Inc.
500 Fifth Avenue, Suite 1600
New York, NY 10110
(212)840-0097